

## AMENDMENT AND RESPONSE UNDER 37 CFR § 1.116 - EXPEDITED PROCEDURE

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Dkt. 267.011US1

Serial Number: 09/702068

Filing Date: October 30, 2000

Title: Enzymatic Treatment of Whey Proteins for the Production of Antihypertensive Peptides and the Resulting Products

IN THE CLAIMS

Please amend the claims as follows.

1. (Currently Amended) A process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising:

(a) preparing an aqueous solution of a whey protein fraction and a proteolytic enzyme, wherein the proteolytic enzyme is trypsin;

(b) holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity;

(c) stopping the reaction; and

(d) drying said hydrolysate to provide the ACE-inhibiting composition, wherein said composition comprises a mixture of peptides having following molecular weight profile, as determined by HPLC

<u>Range (Daltons)</u>	<u>Soluble Peptides</u>
<u>&gt; 5000</u>	<u>50 - 55%</u>
<u>2000 - 5000</u>	<u>15 - 20%</u>
<u>&lt; 2000</u>	<u>30 - 35%</u>

2. (Currently Amended) A The process according to claim 1 wherein the proteolytic enzyme trypsin is inactivated following hydrolysis.

3. (Currently Amended) A The process according to claim 1 wherein the proteolytic enzyme trypsin is inactivated by heating following hydrolysis.

4. (Canceled).

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5. (Currently Amended) An ACE-inhibiting composition as prepared according to claim 1 that comprises a mixture of peptides having the following molecular weight profile, as determined by HPLC

<u>Range (Daltons)</u>	<u>Soluble Peptides</u>
<u>&gt; 5000</u>	<u>50 - 55%</u>
<u>2000 - 5000</u>	<u>15 - 20%</u>
<u>&lt; 2000</u>	<u>30 - 35%</u>

6. (Withdrawn) A treatment regimen for a mammal to inhibit angiotensin-converting enzyme (ACE), said regimen comprising:  
orally administering to the mammal, the composition of claim 5 or 32 in amounts and at intervals effective to ~~inhibit~~ reduce ACE activity.
7. (Canceled)
8. (Currently Amended) ~~A~~ The process according to claim 1, wherein said whey protein fraction is a whey protein isolate.
9. (Currently Amended) ~~A~~ The process according to claim 1, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 5.5 to 6.5%.
10. (Currently Amended) ~~A~~ The process according to claim 1, wherein said whey protein fraction is produced by ion exchange and is characterized by a protein content of at least 94% and an ash content of less than 3%.

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11. (Currently Amended) ~~A~~ The process according to claim 10, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 5.5 to 6.5%.

12. (Currently Amended) A process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising:

(a) preparing an aqueous solution of a whey protein fraction produced by ion exchange and a ~~proteolytic enzyme, wherein the proteolytic enzyme is trypsin;~~

(b) holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity;

(c) stopping the reaction when a degree of hydrolysis is reached within the range of from 5.5 to 6.5%, wherein said hydrolysate comprises a mixture of peptides having is characterized by the following Molecular Weight Profile, as determined by HPLC (HPLC)

Range (Daltons)	Soluble Peptides
> 5000	50 - 55%
2000 - 5000	15 - 20%
< 2000	30 - 35%; and

(d) drying said hydrolysate to provide the ACE-inhibiting composition.

13. (Currently Amended) A process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising:

a) preparing an aqueous solution of trypsin and a whey protein fraction, prepared by ion exchange processing and characterized by a protein content of at least 94% and an ash content of less than 3%, ~~and trypsin;~~

b) holding said aqueous solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate;

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c) stopping said reaction to provide a hydrolysate solution; and  
d) drying said hydrolysate solution prepared in step c to provide the ACE-inhibiting composition, wherein said composition comprises a mixture of peptides having the following molecular weight profile, as determined by HPLC

<u>Range (Daltons)</u>	<u>Soluble Peptides</u>
<u>&gt; 5000</u>	<u>50 - 55%</u>
<u>2000 - 5000</u>	<u>15 - 20%</u>
<u>&lt; 2000</u>	<u>30 - 35%</u>

14. (Canceled)

15. (Currently Amended) A The process according to claim 13, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 5.5 to 6.5%.16. (Currently Amended) A The process according to claim 1 or 12, wherein the whey protein fraction has an ash content of <3%.17. (Currently Amended) A The process according to claim 1, 12, or 13, wherein the whey protein fraction has a mineral content of calcium of 15-20 meq/kg.18. (Currently Amended) A The process according to claim 1, 12, or 13, wherein the whey protein fraction has a mineral content of magnesium of <1 meq/kg.19. (Currently Amended) A The process according to claim 1 or 12, wherein the whey protein fraction has a protein content of at least 35%.

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20. (Currently Amended) ~~A~~ The process according to claim 1 or 12, wherein the whey protein fraction has a protein content that varies by 0 to 25% from  $97.5 \pm 1.0\%$ .
21. (Currently Amended) ~~A~~ The process according to claim 1 or 12, wherein the whey protein fraction has a protein content that varies by 5 to 10% from  $97.5 \pm 1.0\%$ .
22. (Currently Amended) ~~A~~ The process according to claim 1, 12, or 13, wherein the whey protein fraction has a protein content that varies less than 5% from  $97.5 \pm 1.0\%$ .
23. (Currently Amended) ~~A~~ The process according to claim 1, 12, or 13, wherein the whey protein fraction has a protein content of  $97.5 \pm 1.0\%$ .
24. (Currently Amended) ~~A~~ The process according to claim 1, 12, or 13, wherein the whey protein fraction is characterized as follows:

Analysis	Specification	Typical Range
Moisture (%)	5.0 max	$4.7 \pm 0.2$
Protein, dry basis (N x 6.38)(%)	95.0 min.	$97.5 \pm 1.0$
Fat (%)	1.0 max	$0.6 \pm 0.2$
Ash (%)	3.0 max	$1.7 \pm 0.3$
Lactose (%)	1.0 max	<0.5
pH	6.7 - 7.5	$7.0 \pm 0.2$

25. (Currently Amended) ~~A~~ The process according to claim 12 or 13, wherein the whey protein fraction is a whey protein isolate.

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26. (Currently Amended) ~~A~~ The process according to claim 1, 12, or 13, wherein the ~~proteolytic enzyme~~ trypsin is porcine trypsin.
27. (Currently Amended) ~~A~~ The process according to claim 1, 12, or 13, further comprising concentrating said hydrolysate.
28. (Currently Amended) ~~A~~ The process according to claim 1 or 12, wherein the hydrolysate is spray-dried.
29. (Currently Amended) ~~A~~ The process according to claim 1, wherein the whey protein fraction is prepared by ion-exchange processing.
30. (Currently Amended) ~~A~~ The process according to claim 1, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 11.0-12.5%.
31. (Currently Amended) ~~A~~ The process according to claim 1, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 19.5-20.5%.
32. (Currently Amended) An ACE-inhibiting composition as prepared according to claim ~~12~~ or 13-12, 13, 32 or 33 that comprises a mixture of peptides having the following molecular weight profile, as determined by HPLC

<u>Range (Daltons)</u>	<u>Soluble Peptides</u>
<u>&gt; 5000</u>	<u>50 - 55%</u>
<u>2000 - 5000</u>	<u>15 - 20%</u>
<u>&lt; 2000</u>	<u>30 - 35%</u>

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33. (Cancelled)

34. (Currently Amended) A process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising:

- a) preparing an aqueous solution of a whey protein isolate and trypsin;
- b) holding said aqueous solution under conditions effective for reaction to partially hydrolyze said whey protein isolate;
- c) stopping said reaction to provide a hydrolysate solution; and
- d) drying said hydrolysate solution prepared in step c to provide the ACE-inhibiting composition, wherein the composition comprises a mixture of peptides having the following molecular weight profile, as determined by HPLC

<u>Range (Daltons)</u>	<u>Soluble Peptides</u>
<u>&gt; 5000</u>	<u>50 - 55%</u>
<u>2000 - 5000</u>	<u>15 - 20%</u>
<u>&lt; 2000</u>	<u>30 - 35%</u>

35. (Currently Amended) A The process according to claim 34, wherein the whey protein isolate has a protein content that varies by 0 to 25% from 97.5%.

36. (Currently Amended) A The process according to claim 34, wherein the whey protein isolate has a protein content of at least 94%.

37. (Previously Presented) The process according to claim 34, wherein the whey protein isolate contains at least 70%  $\beta$ -lactoglobulin.

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38. (Previously Presented) The process according to claim 37, wherein the whey protein isolate contains at least 80%  $\beta$ -lactoglobulin.

39. (Previously Presented) The process according to claim 38, wherein the whey protein isolate contains about 91%  $\beta$ -lactoglobulin.